REMARKS

Applicants thank the Examiner for the thorough consideration given the present application.

Claims 1-2, 4-27 and 29-31 are pending. Claims 3 and 28 are cancelled. Claims 1, 2 and 4 are amended. Specifically, amended claim 1 finds support in, for instance, pages 5-7 and Example 3 of the present specification and Fig. 2a. Also, amended claim 2 finds support in, for instance, original claim 2. Claims 30 and 31 are added in a varying scope, support for which can be found on at least page 10, lines 1-4 of the present specification. Thus, no new matter has been added.

Withdrawn claims 9-23 directed to a method for preparing a biochip of claim 1 have not been cancelled. Applicants respectfully request that these method claims be rejoined upon allowance of claim 1.

The Examiner is respectfully requested to reconsider the pending application, as amended.

Objection to claim 2

Regarding the objection to claim 2, this claim have been amended to remove minor informalities. Thus, the objection has been rendered moot.

Issues under 35 U.S.C. § 112, first paragraph

Claims 1-2 and 26-29 have been rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

Specifically, the Examiner objects to the term "free orientation without being immobilized. In response, Applicants have amended claim 1 to recite "free orientation without being covalently bound to the gel".

By way of this submission, the 112, first paragraph rejection has been overcome and withdrawal thereof is respectfully requested.

Issues under 35 U.S.C. §§ 102 and 103

The following rejections are pending:

A) Claims 1-2, 5-6, 8 and 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al. (Biotechnology and Bioengineering, vol. 73, pages 331-337 (5 June 2001)).

B) Claims 1-2 and 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al. (U.S. Patent Application Publication No. US 2002/0015952 A1, publish 7 February 2002).

C) Claims 1-2 and 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Dordick et al. (PCT International Application Publication No. WO 03/038131 A1, published 8 May 2003).

D) Claims 1-2 and 26-27 are rejected under 35 U.S.C. 102(e) as being anticipated by Dordick et al. (U.S. Patent Application Publication No. US 2003/0162284 A1, filed 1 November 2002).

E) Claims 1, 5, 7 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (Biotechnology and Bioengineering, vol. 73, pages 331-337 (5 June 2001) in view of Simon et al. (U.S. Patent No. 5,569,607, issued 29 October 1996).

F) Claims 1, 26-27 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (Biotechnology and Bioengineering, vol. 73, pages 331-337 (5 June 2001) in view of Croxson (U.S. Patent No. 5,108,891, issued 28 April 1992).

G) Claims 5-6 and 8 are rejected under 35 U.S.C. 103(a) as being obvious over Anderson et al. (U.S. Patent Application Publication No. U.S 2002/0015952 A1, published 7 February 2002) in view of Kim et al. (Biotechnology and Bioengineering, vol. 73, pages 331-337 (5 June 2001)).

H) Claims 7 is rejected under 35 U.S.C. 103(a) as being obvious over Anderson et al. (U.S. Patent Application Publication No. US 2002/0015952 A1, published 7 February 2002) in view of Kim et al. (Biotechnology and Bioengineering, vol. 73, pages 331-337 (5 June 2001) as applied to claim 5 above, and further in view of Simon et al. (U.S. Patent No 5,569,607, issued 29 October 1996).

I) Claims 1, 26-27 and 29 are rejected under 35 U.S.C. 103(a) as being obvious over Anderson et al. (U.S. Patent Application Publication No. US 2002/0015952

A1, published 7 February 2002) in view of Croxson (U.S. Patent No. 5,108,891, issued 28, April 1992).

J) Claims 1 and 28 are rejected under 35 U.S.C. 103(a) as being obvious over Anderson et al. (U.S. Patent Application Publication No. US 2002/0015952 A1, published 7 February 2002) in view of Simon et al. (U.S. Patent No. 5,569,607, issued 29 October 1996).

These references are labeled hereinafter using the following D1 to D6.

D1 (Kim et al) Biotechnology and Bioengineering, vol. 73, pages 331-337(5 June 2001)
D2 (Anderson et al) US 2002/0015952, (2002.02.07)
D3 (Dordick at al) WO 03/038131 (2003.05.08)
D4 (Dordick et al) US 2003/0162284 (2002.11.01)
D5 (Simon at al) US 5,569,607 (1996.10.29)
D6 (Croxson) US 5,108,891

Applicants respectfully traverse these rejections.

While not conceding to the Examiner's rejections, but to merely advance prosecution, independent claim 1 has been amended to further emphasize the distinctions between the present invention and the cited art.

The Present Invention and its Advantage

The claimed invention includes a combination of elements and is directed to a biochip comprising: a chip substrate; circular gel spots mounted and immobilized on said chip substrate, wherein said gel spots have pores therein; and biomaterials entrapped in said pores of said gel spots and encapsulated by said gel spots, and said biomaterials have a free orientation without being covalently bound to the gel matrix, wherein, said chip substrate is selected from the group consisting of polymethyl methacrylic acid(PMMA), polycarbonate(PC) and cyclic olefin

copolymers(COC) and coated with a coating agent selected from the group consisting of polyvinyl acetate (PVAc) having a molecular weight in the range of 800 to 200,000, poly(vinyl butyral-co-vinylalcohol-co-vinyl acetate) having a molecular weight in the range of 70,000 to 120,000, poly(methyl methacrylate-co-methacrylic acid) having a molecular weight of 10,000 or more, poly(methyl vinyl ether-maleic anhydride) having a molecular weight of 200,000 or more, poly(methyl vinyl ether-maleic anhydride) having a molecular weight of 1,000,000 or more, poly(methyl acrylate) having a molecular weight of 10,000 or more, 3-glycidoxypropyltrimethoxysilane (GPTMOS), dissolved in solvent(s) selected from the group consisting of methylene chloride, tetrahydrofuran, ethanol, methanol, butanol, methyl ethyl ketone, acetone, isopropyl alcohol, ethyl acetate, methyl isobutyl ketone, and di-acetone alcohol, and wherein, said gel spots are formed by the gelation of a sol mixture on said chip substrate.

In particular, amended claim 1 of the present application has the following features:

(i) Morphology of the spots: the gel spots are circular (see claim 1) and up to 1000 spots/cm^2 can be integrated on a chip substrate (see new claims 30 and 31);

(ii) Type of chip substrate: a plastic chip substrate, such as PMMA, PC, COC, etc.;

(iii) Treatment of the chip substrate: the chip substrate is coated with a specific coating agent which is a sol mixture containing biomaterials. This sol mixture containing biomaterials can be integrated in a spot form on a chip substrate. In addition, even glassy gels containing silicate can be immobilized to the substrate; and

(iv) Mobility of biomaterials: the biomaterials are not immobilized or covalently bound to the gel matrix to thereby have a free orientation.

By way of these features, the biochip according to the present invention provides improved reactivity and sensitivity because a large amount of biomaterials can be contained in gel spots while maintaining its 3-dimensional structure (for example, see page 5, lines 14-22 of the present specification).

Therefore, it is respectfully submitted that amended claim 1 is not anticipated by the cited art as set forth in Section 2131 of the MPEP (Original Eighth Edition, August 2001 Latest Revision August, 2007, page 2100-67) nor rendered obvious as set forth in MPEP2143.

As will be explained below, the cited art does not set forth the features of morphology of the spots, type of chip substrate selected from PMMA, PC and COC, treatment of the chip substrate with coating agent of PVAc and/or biomaterial having a free orientation as defined in the newly amended claim 1.

Distinctions over the Cited Art

(1) As to D1 (Kim)

D1 discloses a method for micro-patterning sol-gel structures containing active protein by **using microchannels** as a mould, and a biochip having sol-gel encapsulated proteins in **a linear shape**. The size of a channel is larger than 500 ㎛ (page 332, Fig. 1, and page 333, Fig. 2(b) of D1).

Consequently, D1 does not teach or suggest the claimed features that the biomaterials are entrapped in pores of gel spots on a chip substrate, wherein the claimed gel spots are integrated in the chip in an amount of up to 1000 spots/cm^2 as recited in claims 1 and 30.

Moreover, D1 is interested mainly in encapsulation within microchanneled sol-gel networks and thus is focused on the structure or size of pores suitable for encapsulating biomaterials. On the other hand, the present invention is further interested in the morphology of the spots formed on the chip substrate.

The inventors have found the adhesion between the spot type of sol mixture and the chip substrate is important. Thus, it is an aspect of the invention to form and maintain the small size of spots in a spherical morphology while maintaining its three-dimensional structure.

By the chip substrate surface treatment with a specific coating agent for a chip substrate, a sol mixture containing biomaterials can be integrated in a spot form on a chip substrate. Then, the sol-gel reaction to gel the sol mixture can occur on a chip substrate, and thus a sol-gel matrix can be immobilized on the chip substrate. In other words, when the claimed coating agent is coated to the chip substrate, the gelation on the chip substrate is promoted. The gel state is not separated during assay on an aqueous phase including antigen-antibody reaction and in severe washing after the gelation. Thus, coating which is of hydrophobic nature can maintain the shape of spots. For example, reference is made to page 6, lines 13-16 of the present specification.

Besides, when a sol mixture or gel containing biomaterials is formed and maintained in a shape of spots on a chip substrate, the following advantageous effect can be achieved:

1. As described in Step 3 of Example 2 of the present invention, it is possible to integrate a sol mixture containing biomaterials into circular spots having a diameter of 100 to500 μm on the chip substrate, by using an inkjet integration program of the Arrayer (page 13, line s 24-26), thereby facilitating the preparation of a biochip and allowing computerized manipulation. Briefly, the micro-array type of biochip wherein spots are integrated by an

inkjet array manner is economical and productive, thereby allowing High Throughput Screening (HTS) and commercialization profitably (In more detail, see Example 3 of the present specification).

2. The present invention can integrate various types of proteins, antigens, antibodies, low molecular materials, and bacteria in spots of 10,000 or more on one chip. As shown in Fig. 7b, the present invention can diagnose a marker for diagnosis of general cancers and concurrently a marker for diagnosis of a specific cancer (See, for example, paragraph [00 72] of the present specification).

As discussed above, it is evident that D1 does not teach or suggest that the biomaterials are entrapped in pores of gel spots on a chip substrate (see claim 30), by means of which up to 1000 spots/cm^2 can be integrated on a chip substrate, and that various types of proteins, antigens, antibodies, low molecular materials, and bacteria can be integrated in spots of 10,000 or more at on one chip. Therefore, the subject matter of claims 1 is neither anticipated by nor rendered obvious over D1.

(2) As to D2 (Anderson)

D2 is directed to a fiber bundle comprising a plurality of fibers attached to each other in a fixed position with respect to each other wherein the fibers have different agents of interest immobilized in or on different fibers. That is, D2 relates to micro-well type of chips.

However, D2 fails to disclose or suggest the claimed features including morphology of the spots, type of chip substrate selected from PMMA, PC and COC, treatment of the chip

substrate with coating agent of PVAc and/or biomaterial having a free orientation without a covalent bond as defined in at least claim 1.

Specifically, as illustrated in the following Fig. 1 of D2, a rod or tube 1 incorporates an agent of interest. The rods or tubes may be bonded into a flat parallel array 2, and multiple flat arrays then are bonded into the multiple parallel bundles 3.

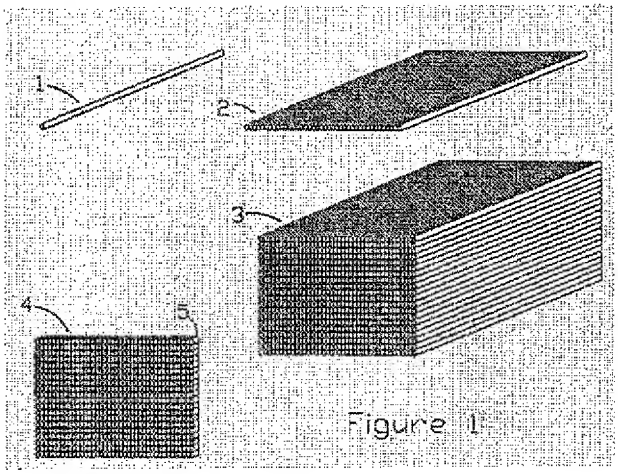

Figure 1

Also, Area 13 in Fig. 2 of D2 is shown additionally, which is enlarged as a reference number 14 to illustrate the presence of immobilized reactants 15 (corresponds to "biomaterials" of the present invention) on the surface of the exposed particles 12 (corresponding to "gel spots" of the present invention).

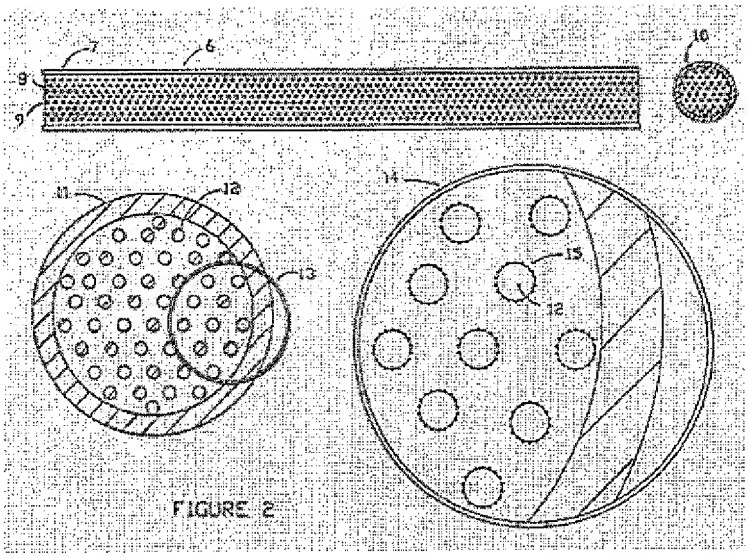

FIGURE 2

According to D2, the exposed particles 12 substantially have a form of linear tubules (rod or tube). Thus, it is not formed on the chip substrate in form of circular gel spots (as recited in claim 1). Further, the reactants 15 of D2 are immobilized in the tubules abs as such, cannot have a free orientation. In this context, the biomolecules of D2 are chemically and thermally stabilized when they are immobilized on a sol-gel matrix (See Dave et al. [Anal. Chem. 66:1120, 1994]). "*The key agent of interest components of the fibers is retained by the fiber by* ***being immobilized*** *therein*" (See, paragraph [0188] of D2).

Moreover, D2 does not disclose a plastic substrate and coating treatment thereof. In this respect, paragraph [00235] of D2 defines that *the term "substrate" refers to the* ***glass capillary arrays*** *with "major surfaces" referring to the open ends of the channel plate*"

Therefore, the claimed invention is patentably distinct from D2 in that (i) the tubules of D2 do not have a form of gel spots, (ii) the biomaterials of D2 are immobilized in the tubules and thus cannot have a free orientation, and (iii) only glass capillary arrays of D2 are disclosed as a

substrate. Thus, the claimed invention is neither anticipated by nor rendered obvious over the D2 reference.

(3) As to D3 & D4 (Dordick)

D3 and D4 are directed to an apparatus comprising a plurality of independent, permeable micromatrices, wherein each said micromatrix encapsulates at least one test composition, and said plurality of independent micromatrices are fixed on a solid support and are spatially separated.

However, D3 and D4 fail to disclose or suggest the claimed features including morphology of the spots, type of chip substrate selected from PMMA, PC and COC, treatment of the chip substrate with coating agent of PVAc and/or biomaterial having a free orientation as defined in at least claim 1.

Specifically, D3 and D4 disclose a flat, thin solid, such as a glass microscope slide or a silicon wafer, as the solid support (corresponds to 'substrate' of the present invention).

Therefore, the present invention using a plastic substrate coated with a specific coating agent is patentably distinct from D3 and D4. Accordingly, the claimed invention is neither anticipated by nor made obvious over the D3 and D4 references.

(4) As to D5 (Simon) & D6 (Croxon)

The secondary D5 and D6 references cannot make up for the deficiencies of the primary reference D1 as discussed above. Also, D5 and D6 references do not disclose a biochip in which circular gel spots are mounted and immobilized on a plastic chip substrate coated with a specific

coating agent and biomaterials are entrapped in said pores of said gel spots and encapsulated by said gel spots, and said biomaterials have a free orientation without being immobilized.

As explained above, D1-D6 singly or in combination neither suggest nor teach the technical idea of the biochip in which circular gel spots are formed by the gelation of a sol mixture and immobilized on a plastic chip substrate coated with a specific coating agent and the biomaterials are entrapped in pores of the spot and are thereby encapsulated and have a free orientation without being covalently bound to the gel matrix.

By way of the claimed features, the biochip according to the present invention has superior properties in view of reactivity and sensitivity, as confirmed in Experiments 1-5 of the present specification. Accordingly, the present invention is neither anticipated by nor rendered obvious over D1-D6 singly or in combination.

In light of the above remarks, since the amended independent claim 1 of the present application are believed to overcome the 35 USC §§ 102(b) and § 103(a) rejections, the dependent claims therefrom including new claims 31 and 32 are also believed to address the same prior art rejections. Therefore, the Examiner is respectfully requested to withdraw these rejections.

Conclusion

In view of the above remarks, it is believed that all pending claims are allowable.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie, Reg. No. 42,874 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§ 1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By _____

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